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REMARKS

This amendment is in response to the Final Office Action dated April 10, 2006. By said Office Action, claims 5-14 were rejected under 35 USC § 103(a), as being unpatentable over Altman et al. (Proc. Nat. Acad. Sci. USA; 1993, 90: 10330-10334) in view of Matsumura et al. [J. Biol. Chem.; 1992, 267 (33): 23589-23595].

In a telephone interview graciously granted by the Examiner, Applicant proposed to amend claim 5 to better define the claimed method to a complex which is "thermally stable at a temperature of 60 °C", which could not be obtained by the combined teachings of the cited prior art.

In said interview, the Examiner indicated that such proposed amendments will be reconsidered along with Applicant arguments.

Claims 1-14 are in this case. Claims 1-4 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 6 and 15 have been canceled. Claims 5-14 have been rejected. Claim 5 is currently amended.

35 U.S.C. § 103(a) Rejections - Altman in view of Matsumura

The Examiner has rejected claims 5-14 under 35 U.S.C. § 103(a) as being unpatentable over Altman et al. in view of Matsumura et al. The Examiner states that Altman teaches the production of soluble MHC class II complexes in E. Coli. The Examiner further states that Altman teaches that production of empty MHC class I molecules is inhibited by the instability of the complex at physiological temperatures. The Examiner further states that Matsumura teaches the production of MHC class I in *Drosophila melanogaster* cells and that it would have been obvious to a person having ordinary skill in the art to use the method of Altman to produce the MHC class I molecules of Matsumura in E. Coli. In addition, the Examiner states that it is well known that E. Coli can be easily cultivated at temperatures at least as low as 4 °C, which is a temperature not exceeding 60 °C. The Examiner's rejection is respectfully traversed. Claim 5 has now been amended.

As argued in response to Office Action dated July 28, 2004, the MHC class II complexes generated by Altman in bacterial cells or the MHC class I complexes generated by Matsumura in eukaryotic cells were completely unstable at

physiological temperatures of 37 °C let alone at higher temperatures such as at 60 °C as shown for the MHC-I-peptide complex of the instant application (see Figures 4, 7-10 and Example 1 of the Examples section of the instant application). In the Altman study the α and β subunits were synthesized as inclusion bodies in two separate *E. coli* transformants (Ec-I-E^k α and β); following expression, the subunits were re-folded *in vitro* in the presence of an antigenic peptide to form a complex which was stable only at a restricted range of pH conditions, i.e., pH 7.4 - 7.6, and at limited temperatures (i.e., 15 to 25 °C) and was completely unstable at a temperature of 37 °C (see Figure 1b in Altman et al., 1993). On the other hand, Matsumura generated a truncated H-2Kb cDNA encoding the $\alpha 1\alpha 2\alpha 3$ extracellular domains and a full-length murine $\beta 2m$ cDNA and co-transfected these two separate clones into eukaryotic cells (S2/M3 *Drosophila melanogaster* cells). However, the yield of the soluble complexes was extremely low as evidenced by the need to use immunoprecipitation with the Y-3 antibody in order to visualize the recombinant class I complex (see Figures 1c and d in Matsumura). In addition, as is further shown in Figure 1c in Matsumura et al., in the presence of 1 % Triton detergent (which was used to release the MHC complex from the aggregates) the purified class I MHC complex was completely unstable at temperatures higher than 32 °C (e.g., 37, 42 and 47 °C). These results therefore demonstrate that Matsumura et al. were unable to form a stable class I MHC complex in the eukaryotic system and therefore one of ordinary skill in the art would not have been motivated to use the teachings of Altman and Matsumura to arrive at a method of producing MHC class I-antigenic peptide complex in a prokaryotic expression system which results in a thermally stable complex at a temperature of 60 °C.

Applicant has elected to amend claim 5 such that it claims the production of MHC class I-antigenic peptide complexes which are thermally stable at a temperature of 60 °C and as such could not have been generated using the combined teachings of Altman and Matsumura.

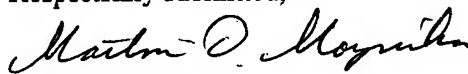
Support for this claim language can be found in Page 54 lines 18-19 and Page 55 lines 1-5 of the instant application, in which the thermal stability of the MHC class I-antigenic peptide complex was shown by incubating the MHC class I-G9-209-2M complex under extreme temperatures (i.e., up to 80 °C). The functional and thermally

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stable MHC class I-antigenic peptide complex of the present invention retained its specific pattern of secondary structure up to a temperature of 60 °C as was revealed by the melting curve of the G9-209-containing MHC-peptide complex using circular dichroism (CD) spectroscopy assay. "The melting curve showed that the complex containing peptide G9-209-2M was thermally stable with a melting temperature of approximately 60 °C".

In view of the claim amendments and accompanying arguments, Applicant believes that claims 5-14 are no longer rendered obvious by the prior art cited by the Examiner. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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